Proposed Registration Decision PRD2016-05

Fluopyram

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Overview

Proposed Registration Decision for Fluopyram

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Fluopyram Technical Fungicide and three end-use products, Luna Privilege containing the technical grade active ingredient fluopyram, Luna Tranquility Fungicide containing the technical grade active ingredients fluopyram and pyrimethanil, and Propulse Fungicide containing the technical grade active ingredients fluopyram and prothioconazole. All three end-use products are used to control several fungal diseases on various horticultural and field crops.

Fluopyram Technical Fungicide (Registration Number 30508), Luna Privilege (Registration Number 30509), Luna Tranquility Fungicide (Registration Number 30510) and Propulse Fungicide (Registration Number 30511) are conditionally registered in Canada. The detailed review for Fluopyram Technical Fungicide, Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide can be found in Evaluation Report ERC2014-02 – *Fluopyram*, with additional updates in this document. The current applications were submitted to convert Fluopyram Technical Fungicide, Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Fluopyram Technical Fungicide, Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "... the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on Fluopyram, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on Fluopyram, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document as well as Evaluation Report ERC2014-02, *Fluopyram*.

What Is Fluopyram?

Fluopyram is a new conventional fungicide active ingredient. It is a systemic broad-spectrum fungicide to be applied as a foliar spray or through drip irrigation systems on various horticultural and field crops. It acts on fungal pathogen cells by inhibiting their normal respiration process.

Health Considerations

Can Approved Uses of Fluopyram Affect Human Health?

Products containing fluopyram are unlikely to affect your health when used according to label directions.

Potential exposure to fluopyram may occur through the diet (food and water), when handling and applying the products or when entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the acute toxicity of fluopyram was low via the oral, dermal and inhalation routes of exposure. Fluopyram was minimally irritating to the eyes and non-irritating to the skin and did not cause an allergic skin reaction.

The acute toxicity of the end-use product Luna Privilege was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and non-irritating to the skin and did not cause an allergic skin reaction. Both end-use products Luna Tranquility Fungicide and Propulse Fungicide were of low acute toxicity via the oral, dermal and inhalation routes of exposure. They were non-irritating to the eyes and skin and did not cause allergic skin reactions.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests were assessed for the potential of fluopyram to cause neurotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, genetic damage and various other effects. The most sensitive endpoints used for risk assessment were decreased activity and effects on the liver, thyroid and kidneys. There were no indications that the young were more sensitive to fluopyram than the adult animal. Fluopyram caused liver tumours in rats and thyroid tumours in mice at high dose levels. The risk assessment protects against these and any other potential effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and drinking water are not of health concern.

Aggregate chronic (cancer and non-cancer) dietary intake estimates (food plus water) revealed that the general population and infants less than one year old, the subpopulation which would ingest the most fluopyram relative to body weight, are expected to be exposed to less than 64% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluopyram is not of health concern for all population subgroups. The lifetime cancer risk from the use of fluopyram is not of health concern.

Aggregate acute dietary intake estimates (food and water) for the general population and all population subgroups were less than 10% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was children 1-2 years old.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

For the MRLs for this active ingredient, please refer to the Maximum Residue Limit Database on the Maximum Residue Limits for Pesticides webpage.

Some of the fluopyram products are also formulated with the active ingredients pyrimethanil or prothioconazole. These co-active ingredients are already registered for use in Canada.

Occupational Risks from Handling Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide

Occupational risks are not of concern when products containing fluopyram are used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply fluopyram as well as field workers re-entering freshly treated fields can come in direct contact with fluopyram residues on the skin. Therefore, the labels specify that anyone mixing/loading and applying products containing fluopyram must wear a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the anticipated exposure period for handlers and workers, health risks to these individuals are not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Risks in Residential and Other Non-Occupational Environments

Residential health risks are not of concern when commercial products containing fluopyram are applied in residential areas and used according to the label directions.

Environmental Considerations

What Happens When Fluopyram Is Introduced Into The Environment?

When used according to label directions, fluopyram is not expected to pose an unacceptable risk to the environment.

Fluopyram can enter the environment when it is applied as a fungicide on field crops. Fluopyram does not breakdown readily in soils and therefore has the potential for residue carry over to the following crop season. It is moderately mobile in soils and has a potential to move downward through the soil and contaminate groundwater. Fluopyram is unlikely to enter the atmosphere and be transported to areas far removed from where it was applied. Fluopyram is not expected to accumulate in the tissues of organisms.

When used according to the label directions, Fluopyram does not present an unacceptable risk to birds, small mammals, fish, algae, earthworms, bees, invertebrates and aquatic plants. The use of the end-use products, Luna Privilege, Luna Tranquility and Propulse Fungicide, may pose a risk to non-target terrestrial plants and amphibians. Spray buffer zones are specified on the product

label to protect terrestrial and freshwater habitats adjacent to treated areas and specific instructions are provided to prevent runoff into aquatic habitats. Precaution statements are also specified on the product label to inform users that fluopyram can be toxic to terrestrial plants and amphibians.

Value Considerations

What Is the Value of Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide?

Luna Privilege Fungicide, Luna Tranquility Fungicide and Propulse Fungicide provide effective solutions for the management of major economic diseases such as powdery mildew, moulds, blights and other foliar diseases on a range of crops including potato, dry bean, chickpeas, lentils, apple, cherry, wine grape, strawberry, peanut, watermelon and almond. The combinations of different modes of action in Luna Tranquility Fungicide (fluopyram and pyrimethanil) and Propulse Fungicide (fluopyram and prothioconazole) are of value in reducing the risk of resistance development and by increasing the spectrum of disease protection.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health
Because there is a concern with users coming into direct contact with fluopyram residues on the skin, anyone mixing, loading and applying products containing fluopyram must wear a long-sleeved shirt, long pants, shoes plus socks, and chemical resistant gloves.

Environment
To minimize potential risks to non-target terrestrial plants and amphibians, label statements and no-spray buffer zones to protect sensitive terrestrial and aquatic habitats are specified on the end-use product label.

To mitigate potential exposures via spray drift, no-spray buffer zones of 1 to 15 metres are specified on the end-use product label to protect sensitive terrestrial and amphibian habitats.

Next Steps

Before making a final registration decision on fluopyram, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on fluopyram (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Fluopyram

1.0 The Active Ingredient, its Properties and Uses

1.1 Identity of the Active Ingredient

Details on the identity of the active ingredient can be found in ERC2016-02, *Fluopyram*.

1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product

Details on the properties and uses can be found in ERC2016-02.

1.3 Directions for Use

Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide are used for the control of powdery mildew, moulds, blights and other foliar diseases on various field and horticultural crops. The products are intended for foliar applications on all crops with the exception of strawberry where applications via chemigation are indicated for Luna Privilege. The application rate ranges for Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide, are 150-500 mL/ha, 600-1200 mL/ha and 500-750 mL/ha, respectively.

1.4 Mode of Action

Details on the mode of action of fluopyram can be found in ERC2016-02.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

Details on the methods of analysis can be found in ERC2016-02.

2.2 Method for Formulation Analysis

Details on the methods for formulation of analysis can be found in ERC2016-02.

2.3 Methods for Residue Analysis

Please refer to ERC2016-02 for a summary of the previously reviewed data on residue analytical methods for data generation and enforcement purposes. The information captured herein relates only to the scientific rationale provided to the Agency in support of the conversion from conditional to full registration. The rationale regarding analytical methodology was presented to support the Multiresidue Method DFG S19 as the enforcement method for fluopyram residues in plant matrices, in lieu of independent laboratory validation of Method GM-001-P017-01.

Multiresidue Method DFG 019, a gas chromatography method with mass spectrometric detection (GC-MS) was proposed for enforcement purposes in plant commodities (Appendix II, Table 1). The method fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70-120%) were obtained in plant matrices. The method was successfully validated in several plant matrices by an independent laboratory. Extraction solvents used in the method were comparable to those used in the metabolism studies, with bridging data provided, thus, further demonstration of extraction efficiency with radiolabelled crops was not required for Multiresidue Method DFG 019.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Please refer to ERC 2018-02 for a summary of the previously reviewed toxicology data for fluopyram, as well as the toxicology endpoints for use in the human health risk assessment.

Cancer Assessment

Tumours were observed in the mouse and the rat in the dietary oncogenicity studies, with treatment-related increases in thyroid follicular cell adenomas in male mice, and liver adenomas and carcinomas in female rats.

In ERC 2018-02, a q_1^* was established as a measure of potency for the tumours observed with oral administration of fluopyram. The document cited further data that would be needed to establish a mode of action (MOA) for each of the thyroid and liver tumours in order to support a threshold approach to cancer risk assessment, rather than the conservative linear low dose extrapolation (q_1^*) that was employed.

In response, the Registrant generated and submitted additional toxicological data, which were found to be acceptable and supported the proposed MOAs for tumour development. On the strength of the collective toxicological data, it was determined that a threshold approach was appropriate for cancer risk assessment for the observed thyroid tumours in mice and liver tumours in rats. Overall, the endpoints selected for non-cancer risk assessment, as reported in ERC 2018-02, are considered to be protective of these findings.

Incidence Reports

Since 26 April 2007, registrants have been required by law to report pesticide incidents to the PMRA that are related to their products. In addition, the general public, medical community, government and non-governmental organizations are able to report pesticide incidents directly to the PMRA. As of 27 May 2019, no human or domestic animal incident reports involving fluopyram have been submitted to the PMRA.

3.1.1 *Food Commodity Residues in Mammalian Toxicology*

Please refer to ERC 2018-02 for a summary of the previously reviewed data.

3.2 [redacted]

Please refer to ERC 2016-02 for a summary of the previously reviewed data.

3.3 [redacted]

Please refer to ERC 2016-02 for a summary of the previously reviewed data.

3.4 [redacted]

3.4.1 [redacted]

Please refer to Section 3.1 above and ERC 2016-02 for a summary of the previously reviewed data.

3.4.1.1 [redacted]

Please refer to ERC 2016-02 for a summary of the previously reviewed data.

3.4.2 [redacted]

3.4.2.1 [redacted]

3.4.2.2 [redacted]

Please refer to ERC 2016-02 for a summary of the previously reviewed data.

Subsequent to ERC 2016-02 , the registrant provided additional toxicity data that supported a threshold approach to cancer risk assessment (refer to Section 3.1). As such, the endpoints selected for worker risk assessment are also protective of any potential cancer findings and there are no health risks of concern.

3.4.3 [redacted]

3.4.3.1 [redacted]

There are no domestic products, therefore no residential mixer/loader/applicator risk assessment is required.

3.4.3.2 [redacted]

Please refer to ERC 2016-02 for a summary of the previously reviewed data.

Subsequent to ERC 2016-02 , the registrant provided additional toxicity data that supported a threshold approach to cancer risk assessment (Refer to Section 3.1). As such, the endpoints selected for risk assessment for the general population entering pick-your-own (PYO) areas treated with fluopyram are also protective of any potential cancer findings and there are no health risks of concern.

3.4.3.3 Bystander Exposure and Risk

Please refer to ERC2014-02 for a summary of the previously reviewed data.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

Please refer to ERC2014-02 for a summary of the previously reviewed data and the rationale for the regulatory decision. The information captured herein relates only to the scientific rationale provided to the Agency in support of the conversion from conditional to full registration. The rationale regarding field accumulation studies was presented in lieu of the field rotational crop data on canola, soybean and cereals. The change in the chronic cancer dietary exposure results due to the modification of the approach for cancer risk assessment for fluopyram (refer to Section 3.1) is also addressed herein.

As the primary crop uses and the rotational crop restrictions on the labels remain the same, and they do not present health risks of concern from a dietary exposure perspective, crop field trials conducted throughout Canada and the United States using end-use products containing fluopyram at exaggerated rates in or on canola, soybeans, wheat and corn (field and sweet) are sufficient to support the established maximum residue limits in/on these rotational crops when the end-use products are used according to label directions, including the specified plant-back intervals.

3.5.2 Exposure from Drinking Water

3.5.2.1 Concentrations in Drinking Water

Refer to ERC2014-02 for details on concentrations in drinking water. Level 1 concentrations found in Table 13 of ERC2014-02 were used to conduct the drinking water risk assessment for the conversion from conditional to full registration. These Level 1 concentrations were used in reassessing the dietary risk for the conversion from conditional to full registration.

3.5.3 Dietary Risk Assessment

Acute and chronic (cancer and non-cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™).

3.5.3.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the refined chronic cancer and non-cancer analysis for fluopyram: Supervised trial mean residue (STMR) values, experimental processing factors where available, Canadian and American projected percent crop treated values, and anticipated residues for livestock commodities. The refined chronic dietary exposure from all supported fluopyram food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 7% of the ADI. Aggregate exposure from food and water is considered acceptable.

The PMRA estimates that chronic dietary exposure to fluopyram from food and water is 19.6% (0.002350 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for infants less than one year old at 63.8% (0.007661 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

The following criteria were applied in the basic acute analysis for fluopyram: 100% crop treated, default processing factors, and residues of fluopyram in/on crop and animal commodities at MRL levels. The basic acute dietary exposure from all supported fluopyram food uses was estimated to be 4.4% of the ARfD for the general population (95th percentile, deterministic). Aggregate exposure from food and water is considered acceptable and below PMRA's level of concern. Specifically, an acute dietary exposure of 2.8% to 9.8% of the ARfD was obtained for all population subgroups, with children 1-2 years old as the highest exposed population subgroup. Please refer to ERC2014-02 for details.

3.5.4 Aggregate Exposure and Risk

The aggregate risk for fluopyram consists of exposure from food and drinking water sources only. Given that apples and strawberries can be treated with fluopyram, there is potential for exposure during pick-your-own harvesting activities and during harvesting of fruit from trees, in residential settings, that may have been treated. Since the acute dietary and short-term dermal toxicological endpoints are based on different toxicological effects, no aggregation of dermal and dietary exposure is required. Please refer to ERC2014-02 for details.

3.5.5 Maximum Residue Limits

Please refer to the Maximum Residue Limit Database on the Maximum Residue Limits for Pesticides webpage for the MRLs for this active ingredient. Please refer to ERC2014-02 for the nature of the residues in animal and plant matrices, analytical methodology and field trial data for fluopyram. The acute and chronic (cancer and non-cancer) dietary risk estimates are summarized in Appendix I, Table 2.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Refer to ERC2014-02 for details on fate and behaviour of fluopyram in terrestrial and aquatic systems.

4.2 Environmental Risk Characterization

Refer to ERC2014-02 for details on environmental risk characterization from the use of fluopyram.

4.2.1 Risks to Terrestrial Organisms

Refer to ERC2014-02 for details on risk to terrestrial organisms from the use of fluopyram.

4.2.2.1 Risks to Aquatic Organisms

Refer to ERC2014-02 for details on risk to aquatic organisms from the use of fluopyram.

5.0 Value

5.1 Consideration of Benefits

The addition of fluopyram as another chemical control option will potentially increase the longevity of other products with different modes of action as viable options for specific disease control. Combining chemical control with other cultural or biological control measures should minimize the dependence on any one control measure and therefore minimize the potential for resistance or increased tolerance to develop to any one control measure.

Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide are not phytotoxic to labelled crops and fit well into current IPM strategies when used according to directions. These broad spectrum products will benefit fruit and vegetable producers and offer a useful alternative in disease resistance management. In addition, because Luna Tranquility Fungicide and Propulse Fungicide each combine two active ingredients with different modes of action, the risk of disease resistance development is reduced in targeted pathogens that are sensitive to the two active ingredients.

Several alternatives exist for most disease claims/crop combinations. The chemical and other non-conventional/biological fungicidal active ingredients listed in Appendix I, Table 3, are found in products that are registered for control or suppression of diseases indicated on the Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide labels.

5.2 Effectiveness Against Pests

Following the review of the original submission to register fluopyram and the associated end-use products, it was determined that confirmatory value information was required to support two claims: powdery mildew on standard sized cherry trees and late leaf spot on peanuts, as identified in ERC2014-02. These claims were withdrawn from the label at the request of the registrant and therefore no further value information was required.

Review results for the remaining claims can be found in ERC2014-02.

5.3 Non-Safety Adverse Effects

Phytotoxicity was not observed from any of the three products when applied at rates consistent with their labelled use patterns.

5.4 Supported Uses

Details of the supported uses are provided in Appendix I, Tables 4, 5 and 6.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

Please refer to ERC2014-02 for details.

6.2 Formulants and Contaminants of Health or Environmental Concern

Please refer to ERC2014-02 for details.

7.0 Summary

7.1 Human Health and Safety

Mixers, loaders and applicators handling products containing fluopyram and workers re-entering treated areas and patrons entering pick-your-own (PYO) areas are not expected to be exposed to levels of fluopyram that will result in health risks of concern when the products are used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

The nature of the residues in plants and animals is adequately understood. The residue definition for enforcement is fluopyram in plant products and fluopyram including the metabolite fluopyram-benzamide in animal matrices. The approved uses of fluopyram on watermelon, wine grapes, strawberries, dry beans, dry chickpeas, dry lentils, peanuts, apples, potatoes, cherries and almonds do not constitute an acute or chronic (cancer and non-cancer) dietary risk (food and drinking water) of concern to any segment of the population, including infants, children, adults and seniors. For the MRLs for this active ingredient, please refer to the Maximum Residue Limit Database on the Maximum Residue Limits for Pesticides webpage.

For full details, please refer to ERC2014-02.

7.2 Environmental Risk

Please refer to ERC2014-02 for details.

7.3 Value

Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide provide effective solutions for the management of major economic diseases such as powdery mildew, moulds, blights and other foliar diseases on a range of crops including potato, dry bean, chickpeas, lentils, apple, cherry, wine grape, strawberry, peanut, watermelon and almond. The combinations of different modes of action in Luna Tranquility Fungicide and Propulse Fungicide are of value in reducing the risk of resistance development and by increasing the spectrum of disease protection.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Fluopyram Technical Fungicide and end-use products, Luna Privilege containing the technical grade active ingredient fluopyram, Luna Tranquility Fungicide containing the technical grade active ingredients fluopyram and pyrimethanil, and Propulse Fungicide containing the technical grade active ingredients fluopyram and prothioconazole. All three end-use products are used to control several fungal diseases on various horticultural and field crops.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

~	not classified
µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
ER_{25}	effective rate for 25% of the population
g	gram
GC-MS	gas chromatography with mass spectrometric detection
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IPM	Integrated pest management
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
M	multi-site mode of action
mg	milligram
mL	millilitre
MAS	maximum average score

MOE	margin of exposure
MOA	mode of action
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PHI	preharvest interval
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PYO	pick-your-own
q_1^*	cancer potency factor
RSD	relative standard deviation
SC	soluble concentrate
STMR	supervised trial mean residue
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
U	Unclassified mode of action
UAN	urea ammonium nitrate
UF	uncertainty factor
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Plant	MultiresidueMethod DFG S19 Enforcement method	Fluopyram	GC-MS	0.01 ppm	Lettuce head, rape seed, wheat grain, orange, pea seed, cabbage head	PMRA# 1599629, 1599871, 1599768

Table 2 Food Residue Chemistry - Risk Assessment

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)	
		Food Only	Food and Water
Refined chronic (cancer and non-cancer) dietary risk ADI = 0.012 mg/kg bw/day Estimated chronic drinking water concentration = 104 µg a.i./L	All infants < 1 year	3.9	63.8
	Children 1-2 years	6.3	33.4
	Children 3-5 years	3.9	29.3
	Children 6-12 years	2.0	19.5
	Youth 13-19 years	0.8	14.0
	Adults 20-49 years	0.8	17.8
	Adults 50+ years	1.0	18.9
	Females 13-49 years	0.8	17.8
	Total population	1.3	19.6
	POPULATION	ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)	
		Food Only	Food and Water
Basic acute dietary exposure analysis, 95th percentile ARfD = 0.5 mg/kg bw Estimated acute drinking water concentration = 106 µg a.i./L	All infants < 1 year	7.0	9.1
	Children 1-2 years	8.8	9.8
	Children 3-5 years	7.5	8.4
	Children 6-12 years	5.3	5.8
	Youth 13-19 years	3.5	3.9
	Adults 20-49 years	2.8	3.3
	Adults 50+ years	2.2	2.8
	Females 13-49 years	2.8	3.3
	Total population	4.4	5.0

Table 3 Active Ingredients Currently Registered for Management of Crop Diseases on the Luna Privilege Fungicide (1), Propulse Fungicide (2), and Luna Tranquility Fungicide (3) Labels (as of September 2015)

Crops	Diseases	Active Ingredients (Resistance Management Group)
WATERMELON	Powdery mildew[1]	extract of *Reynoutria sachalinensis* (–)
		mineral oil (–)
		potassium bicarbonate (–)
		Streptomyces lydicus WYEC 108 (–)
		Bacillus amyloliquefaciens, strain D747 (44)
		Bacillus subtilis QST 713 (44)
		difenoconazole (3)
		myclobutanil (3)
		prothioconazole (3)
		benzovindiflupyr (7)
		fluxapyroxad (7)
		penthiopyrad (7)
		pyraclostrobin (11)
		trifloxystrobin (11)
		chlorothalonil (M5)
		metrafenone (U8)
	Botrytis grey mold[1]	penthiopyrad (7)
WINE GRAPE	Botrytis bunch rot / Grey mold[1,3]	*Aureobasidium pullulans* DSM 14940 and DSM 14941 (–)
		blad polypeptide (–)
		Bacillus amyloliquefaciens, strain D747 (44)
		Bacillus subtilis QST 713 (44)
		fluxapyroxad (7)
		boscalid (7) + pyraclostrobin (11)
		fenhexamid (17)
	Powdery mildew[3]	blad polypeptide (–)
		extract of *Reynoutria sachalinensis* (–)
		garlic powder (–)
		mineral oil (–)
		potassium bicarbonate (–)
		tea tree oil (–)
		Bacillus subtilis QST 713 (44)
		boscalid (7)
		calcium polysulfide (M2)
		copper oxychloride (M1)
		difenoconazole (3)
		flutriafol (3)
		myclobutanil (3)
		benzovindiflupyr (7)
		fluxapyroxad (7)
		kresoxim-methyl (11)
		trifloxystrobin (11)
		pyraclostrobin (11) + boscalid (7)

Crops	Diseases	Active Ingredients (Resistance Management Group)
		quinoxyfen (13)
		copper present as copper octanoate (M1)
		sulphur (M2)
		folpet (M4)
		metrafenone (U8)
DRY BEAN (including chickpea and lentil)	White mold[1,2]	iprodione (2)
		metconazole (3)
		boscalid (7)
		fluxapyroxad (7)
		picoxystrobin (11)
		dicloran (14)
		fluazinam (29)
	Ascochyta blight[1,2]	benzovindiflupyr (7)
		penthiopyrad (7)
		penflufen (7) + trifloxystrobin (11)
		azoxystrobin (11) + difenoconazole (3)
	Mycosphaerella blight[1]	pyraclostrobin (11)
		azoxystrobin (11) + benzovindiflupyr (7)
	Powdery mildew[1]	pyraclostrobin (11)
		azoxystrobin (11) + propiconazole (3)
		azoxystrobin (11) + benzovindiflupyr (7)
	Anthracnose[2]	benzovindiflupyr (7)
		pyraclostrobin (11)
		azoxystrobin (11) + difenoconazole (3)
	Asian soybean rust[2]	flutriafol (3)
		benzovindiflupyr (7)
		penthiopyrad (7)
		azoxystrobin (11)
		picoxystrobin (11)
		pyraclostrobin (11)
PEANUT	Early Leaf Spot[1]	*Bacillus subtilis* QST 713 (44)
		prothioconazole (3)
		penthiopyrad (7)
APPLE	Leaf scab[1,3]	garlic powder (–)
		Bacillus subtilis QST 713 (44)
		thiophanate-methyl (1)
		difenoconazole (3)
		flutriafol (3)
		propiconazole (3)
		benzovindiflupyr (7)
		fluxapyroxad (7)
		penthiopyrad (7)
		boscalid (7) + pyraclostrobin (11)
		cyprodinil (9)
		pyrimethanil (9)
		kresoxim-methyl (11)
		trifloxystrobin (11)
		fluazinam (29)

Crops	Diseases	Active Ingredients (Resistance Management Group)
		copper present as copper octanoate (M1)
		thiram (M3)
		ziram (M3)
		dodine (M7)
	Powdery mildew[7]	extract of *Reynoutria sachalinensis* (–)
		mineral oil (–)
		potassium bicarbonate (–)
		Bacillus subtilis QST 713 (44)
		thiophanate-methyl (1)
		difenoconazole (3)
		fluoxazole (3)
		flutriafol (3)
		myclobutanil (3)
		triforine (3)
		benzovindiflupyr (7)
		fluxapyroxad (7)
		penthiopyrad (7)
		boscalid (7) + pyraclostrobin (11)
		cyprodinil (9)
		kresoxim-methyl (11)
		trifloxystrobin (11)
		calcium polysulphide (M2)
		sulphur (M2)
		chlorothalonil (M5)
		metrafenone (U8)
POTATO	Early blight[1,7]	*Bacillus amyloliquefaciens*, strain D747 (44)
		Bacillus subtilis QST 713 (44)
		difenoconazole (3)
		metconazole (3)
		benzovindiflupyr (7)
		boscalid (7)
		fluxapyroxad (7)
		penthiopyrad (7)
		pyrimethanil (9)
		azoxystrobin (11)
		famoxadone (11)
		pyraclostrobin (11)
		famoxadone (11) + cymoxanil (27)
		zoxamide (22)
		copper – different salts (M1)
		mancozeb (M3)
		metiram (M3)
		captan (M4)
		chlorothalonil (M5)
	Brown leaf spot[7]	benzovindiflupyr (7) + difenoconazole (3)
		azoxystrobin (11) + difenoconazole (3)
	White mold[7]	*Bacillus amyloliquefaciens*, strain D747 (44)
		Bacillus subtilis QST 713 (44)

Crops	Diseases	Active Ingredients (Resistance Management Groups)
		metconazole (3)
		fluxapyroxad (7)
		azoxystrobin (11) + difenoconazole (3)
		fluazinam (29)
	Black dot[1]	azoxystrobin (11)
STRAWBERRY	Powdery mildew[1]	bilaid polypeptide (–)
		citric acid (–) + lactic acid (–)
		extract of *Reynoutria sachalinensis* (–)
		mineral oil (–)
		Streptomyces lydicus WYEC 108 (–)
		tea tree oil (–)
		Bacillus amyloliquefaciens, strain D747 (44)
		myclobutanil (3)
		fluazinam (3)
		tebuconazole (3)
		fluxapyroxad (7)
		boscalid (7) + pyraclostrobin (11)
		pyraclostrobin (11)
		quinoxyfen (13)
		copper present as copper octanoate (M1)
		calcium polysulphide (M2)
		sulphur (M2)
CHERRY	Brown rot blossom blight[1]	bilaid polypeptide (–)
		Bacillus subtilis QST 713 (44)
		iprodione (2)
		tebuconazole (3)
		propiconazole (3)
		boscalid (7)
		fluxapyroxad (7)
		penthiopyrad (7)
		fenhexamid (17)
		sulphur (M2)
		ziram (M3)
		chlorothalonil (M5)
ALMOND	Brown rot blossom blight[1]	bilaid polypeptide (–)
		fluxapyroxad (7)
		penthiopyrad (7)
		chlorothalonil[2] (M5)

[1] claim appears on the Luna Privilege Fungicide label
[2] claim appears on the Propulse Fungicide label
[3] claim appears on the Luna Tranquility Fungicide label
[4] registered for ornamental applications only

Table 8 Luna Privilege Fungicide – Supported Use Claims

Supported Use Claims
To control powdery mildew on watermelon, apply Luna Privilege at a rate of 170–250 mL/ha at seven to fourteen day intervals
To control botrytis grey mold on watermelon, apply Luna Privilege at a rate of 500 mL/ha at seven to ten day intervals
To control botrytis bunch rot / grey mold on wine grape, apply Luna Privilege at a rate of 500 mL/ha at early bloom and at berry touch to bunch closure
To control white mold on dry bean, apply Luna Privilege at a rate of 500 mL/ha at seven to fourteen day intervals
To control ascochyta blight on dry bean, apply Luna Privilege at a rate of 500 mL/ha at ten to fourteen day intervals
To control mycosphaerella blight on dry bean, apply Luna Privilege at a rate of 500 mL/ha at ten to fourteen day intervals
To control powdery mildew on dry bean, apply Luna Privilege at a rate of 170–250 mL/ha at seven to fourteen day intervals
To control early leaf spot on peanut, apply Luna Privilege at a rate of 250–500 mL/ha at a 14 day intervals
To control leaf scab on apple, apply Luna Privilege at a rate of 500 mL/ha at seven to fourteen day intervals
To control early blight on potato, apply Luna Privilege at a rate of 170–500 mL/ha at seven to twelve day intervals
To control powdery mildew on strawberry, apply Luna Privilege at a rate of 500 mL/ha through drip irrigation at five to seven day intervals
To control brown rot blossom blight on sweet and tart cherry, apply Luna Privilege at a rate of 250 mL/ha at fourteen day intervals (limit of three applications)
To control brown rot blossom blight on almonds, apply Luna Privilege at a rate of 250–500 mL/ha at fourteen day intervals

Table 9 Luna Tranquility Fungicide – Supported Use Claims

Supported Use Claims
To control powdery mildew on wine grape, apply Fluopyram/Pyrimethanil 500 SC at a rate of 600 mL/ha at seven to fourteen day intervals (limit of 4 applications)
To control botrytis bunch rot / grey mold on wine grape, apply Fluopyram/Pyrimethanil 500 SC at a rate of 1,200 mL/ha at early bloom and at berry touch to bunch closure
To control powdery mildew on apple, apply Fluopyram/Pyrimethanil 500 SC at a rate of 600 mL/ha at seven to fourteen day intervals (limit of 4 applications)
To control leaf scab on apple, apply Fluopyram/Pyrimethanil 500 SC at a rate of 800 mL/ha at seven to fourteen day intervals (limit of 4 applications)

Table 6: Proposed Pesticide – Supported Use Claims

Supported Use Claims
To control white mold on dry bean, apply Fluopyram/Prothioconazole 400 SC at a rate of 700 mL/ha at seven to fourteen day intervals
To control anthracnose on dry bean, apply Fluopyram/Prothioconazole 400 SC at a rate of 500-700 mL/ha at ten to fourteen day intervals

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Please refer to the Maximum Residue Limit Database on the Maximum Residue Limits for Pesticides webpage for the MRLs for this active ingredient.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

Refer to ERC2014-02 -*Fluopyram*.

2.0 Human and Animal Health

PMRA Document Number	Reference
2452435	2014, Rationale supporting DFG S19 multi-residue method as the fluopyram enforcement method in plant matrices, DACO: 7.2.3
2452433	2014, 30509-Cover Letter-29Aug2014, DACO: 0.8 (OECD)

3.0 Environment

Refer to ERC2014-02 -*Fluopyram*.

4.0 Value

PMRA Document Number	Reference
1599332	2008. Fluopyram 500 SC fungicide (500 g a.i./L fluopyram) for control of Botrytis bunch rot in grape, botrytis grey mould in strawberry and tomato, and *Alternaria solani* in tomato, DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4, IIIA 6.1.2, IIIA 6.1.3, IIIA 6.2.1, IIIA 6.3, IIIA 6.4.1, IIIA 6.4.2, IIIA 6.4.3. 322pp.
1670787	2008. Fluopyram/Prothioconazole Fungicide for Control of Ascochyta Blight of Lentil and Chickpea, Mycosphaerella Blight of Dried Shelled Pea, and White Mold of Dried Shelled Bean and Pea. DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4. 272pp.
1670080	2008. Fluopyram + pyrimethanil 500 SC fungicide (125g a.i./L fluopyram + 375g a.i./L pyrimethanil) for control of listed diseases in grapes and small berries, bulb vegetables, tomatoes, and pome fruit. DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4. 420pp.
1674457	2008. Fluopyram 500 SC fungicide for control of listed diseases in horticulture and field crops, DACO: 10.2.3.3,10.2.3.4,10.3.2,10.4,10.5.1,10.5.2,10.5.4. 851pp.
2046958	2011. Cover Letter for Fluopyram Clarification request Sub No 2008-4863 efficacy data to add drip irrigation strawberries. DACO: 0.8. 2pp.
2046960	2011. Efficacy data. DACO: 10.5. 5pp.
2046961	2011. Efficacy data. DACO: 10.5. 5pp.
2046963	2011. Efficacy data. DACO: 10.5. 7pp.